time is being requested concurrently. Accordingly, a response to this Office Action is now due March 3, 1997.

Please amend the subject application as follows:

In the Claims:

Cancel claims 48 and 50-54, without prejudice.

Add new claim 56 to read as follows:

56. The protein of claim 44 which has the amino acid sequence of Figure 1. --

REMARKS

Reconsideration is requested in view of the above amendments and following remarks. Claims 44-48 and 50-55 were pending in the subject application. Claims 48 and 50-54 have been canceled without prejudice to filing in a future application claiming the benefit of the present application's filing date under 35 U.S.C. §120. Claim 55 was withdrawn from consideration. New claim 56 has been added. Accordingly, claims 44-47 and 55-56 are pending, with claims 44-47 and 56 being under consideration at this time.

Accompanying this Amendment are two Declarations which are:

Declaration [I] of Dr. Werner Lesslauer; and

Declaration [II] of Dr. Werner Lesslauer.

Both of these Declarations were originally filed in connection with the parent application, Application No. 08/095,640, and are hereby made of record in the present application.

35 U.S.C. §101 rejections

Claims 48 and 50-53 were rejected as allegedly being a substantial duplicate of claims 102-109 of co-pending Application No. 08/095,640, now allowed. To obviate this rejection, claims 48 and 50-53 were canceled hereinabove, without prejudice.

Applicants request that all rejections under 35 U.S.C. §101 be withdrawn.

35 U.S.C. §112 rejection

Claim 45 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the word "contains" was recommended to

be replaced with the word "has" since it was alleged that the "insoluble protein as claimed will have the amino acid sequence of Figure 1 and not contain it."

Applicants traverse this rejection. Newly added claim 56 is identical to claim 45, except it uses the term "has" instead of "contains" as recommended by the Patent Office. Therefore, claim 56 is allowable as acknowledged by the Patent Office in paragraph 30 of the Office Action.

Claim 45 has not been changed. The fact that additional amino acids could be added at an end of the amino acid sequence of Figure 1 does not make claim 45 indefinite. Claim 45 is dependent upon claim 44 and contains all of the limitations found therein. Thus, the protein must be homogeneous, insoluble, bind tumor necrosis factor, and have an apparent molecular weight of about 55 kilodaltons on a nonreducing SDS-polyacrylamide gel. Clearly such a claim is definite within the meaning of 35 U.S.C. §112.

Considering the above, applicants request that all rejections under 35 U.S.C. §112 be withdrawn.

35 U.S.C. §102 rejections

The invention of claims 44, 45 and 56 is a homogenous insoluble 55 kD protein which binds human tumor necrosis factor ("TNF"). The invention of claims 46 and 47 is a homogenous insoluble 55 kD protein, or a soluble fragment thereof, which binds human TNF and is recombinantly produced in a host cell from a DNA sequence heterologous to said host cell, which DNA sequence encodes said protein or said fragment.

Claim 54 was rejected under 35 U.S.C. §102 over Stauber et al. (JBC 263(35): 19098-19104), Wallach et al. (EP 0 308 378 A2), and Smith et al. (U.S. Patent No. 5,395,760). Applicants traverse this rejection. However, merely to expedite prosecution, applicants have hereinabove canceled this claim without prejudice to filing such a claim in a further patent application.

In view of the above, applicants request that these rejections under 35 U.S.C. §102 be withdrawn.

Claims 44 and 46 were rejected under 35 U.S.C. §102(e) as allegedly being unpatentable over Smith et al. Applicants traverse this rejection. It is well settled that a

reference on which a §102 rejection is based must describe every element of the invention claimed [see In re Marshall, 198 USPQ 344 (CCPA 1978); Ex parte Levy, 17 USPQ2d 1462 (BPAI 1990)]. Smith does not disclose every element of applicants' claimed protein and therefore cannot form a basis for a §102 rejection. Smith fails to disclose a homogenous insoluble 55 kD protein that binds TNF.

Smith relates to the "mature full-length human TNF-R" which is "a glycoprotein having a molecular weight of about 80 kilodaltons" (see Smith at column 3, lines 47-49). The only mention of a 55 kD TNF-R in Smith is found in the Background of the Invention section describing the prior art. Confusion may have arisen because Figure 2A-2B of Smith and Figure 4 of the subject application (a 75 kD protein) depict almost the same amino acid sequence between amino acid numbers 49-439 and 1-392, respectively. However, applicants are not herein claiming a 75 kD protein. Applicants are claiming a protein having an apparent molecular weight of about 55 kD, such as that described in Figure 1 of the present specification. Because Smith provides no meaningful disclosure with respect to the 55 kD TNF-R, it cannot anticipate applicants' claimed invention.

In view of the above, applicants request that the rejection of claims 44 and 46 based on Smith under 35 U.S.C. §102(e) be withdrawn.

Claims 46 and 47 were rejected under 35 U.S.C. §102(a) over Wallach et al. Applicants traverse this rejection. Wallach does not disclose every element of applicants' claimed protein and therefore cannot form a basis for a §102 rejection. Wallach fails to disclose applicants' claimed homogeneous protein which has an apparent molecular weight of 55 kilodaltons on a nonreducing SDS-polyacrylamide gel, or soluble fragment thereof, both of which bind human tumor necrosis factor and both of which are recombinantly produced in a host cell from a DNA sequence heterologous to said host cell, which DNA sequence encodes said protein or said fragment.

Applicants' claimed protein has a molecular weight of 55 kD on SDS-PAGE after HPLC. The Wallach protein has an entirely different molecular weight of 26-28 kD on SDS-PAGE after HPLC (see Wallach, page 3 lines 50-51 and page 7 line 44 through page 8 line 5). Although applicants' SDS-PAGE is under nonreducing conditions and Wallach's is under reducing conditions, such a difference would not lead to a two-fold difference in apparent molecular weight.

Applicants' claimed protein and the Wallach protein are processed through different preliminary purification steps because the Wallach protein is soluble and isolated from urine and applicants' claimed protein is insoluble and isolated from cell membranes. However, both proteins reach their final phase of purification after HPLC and SDS-PAGE. As stated above, once purified applicants' claimed protein and the Wallach protein are clearly different proteins having different molecular weights.

There is nothing in Wallach to indicate any similarity between these two different proteins other than the ability to bind TNF. That these two physically different proteins merely have a common activity is an insufficient basis for a §102 rejection.

Wallach also does not disclose applicants' claimed soluble fragments. Although the Patent Office correctly points out that applicants' claims 46 and 47 are directed to soluble fragments, such fragments must be derived from applicants' claimed insoluble protein. There is no evidence presented by the Patent Office which shows that applicants' claimed fragments (derived from a protein different from that of Wallach) are the same as Wallach's protein. When proteins are different, there is no reason to suppose that one is a fragment of the other unless the art provides a disclosure supporting such an assertion. Thus, Wallach would not have lead the skilled artisan to

the conclusion that any Wallach protein is a fragment of applicants' claimed insoluble 55 kD protein.

The Patent Office also alleged that the partial sequence of the TNF receptor protein disclosed on page 3 of Wallach is exactly the same as amino acids 12-27 disclosed in applicants' Figure 1. With regard to patentability, this is irrelevant. As stated above, the starting proteins of Wallach and applicants are different. Moreover, there is no evidence that this particular Wallach protein (1) binds human tumor necrosis factor or (2) is recombinantly produced in a host cell from a DNA sequence heterologous to said host cell, which DNA encodes said protein or said fragment, as is required by applicants' claimed invention.

Based on the above, applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 46 and 47 under 35 U.S.C. §102(a).

Supplemental Information Disclosure Statement

Pursuant to 37 C.F.R. § 1.56 and §§ 1.97-1.98, applicants draw the Examiner's attention to the references listed on enclosed form PTO-1449 (copies submitted

herewith). Applicants request that the references cited below and on enclosed form PTO-1449 be made of record in the file of the above-identified application.

Document A5 is U.S. Patent No. 5,359,037 corresponding to Japanese Patent Application No. 128956/90 cited by the Japanese Patent Office in connection with the parent patent application. This patent discloses antibodies to TNF Binding Protein I.

Document B13 is European Publication No. 0 422 339 A1 disclosing TNF inhibitors isolated from urine.

Document C23 is an article by Heller et al. [JBC 265(10): 5708-5717 (1990)] disclosing amplified expression of TNF-R in cells transfected with Epstein-Barr virus shuttle vector cDNA libraries.

Document C24 is an abstract presented by Heller et al. [Napa Valley Conference (1989)] disclosing amplified expression of TNF-R in cells transfected with HELA cell cDNA.

Document C25 is an article by Olsson et al. [Eur. J. Haematol., 42: 270-275 (1989)] disclosing TNF binding protein isolated from urine.

Document C26 is an article by Nophar et al. [EMBO J., 9(10): 3269-3278 (1990)] disclosing soluble forms of tumor necrosis factor receptors.

Consideration of the submitted documents is earnestly solicited.

Based upon the above, applicants request reconsideration, withdrawal of all rejections, and issuance of a Notice of Allowance.

If a telephone conference would be of assistance in furthering prosecution of this application, applicants' undersigned attorney request that he be contacted at the number provided.

No fee, except the fee for a three-month extension of time, is required in connection with the filing of this Amendment. If any fee is deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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